

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



PCT



(43) International Publication Date
25 August 2005 (25.08.2005)

(10) International Publication Number
WO 2005/076984 A3

(51) International Patent Classification:
C07H 21/04 (2006.01) C12Q 1/68 (2006.01)

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(21) International Application Number:
PCT/US2005/003776

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 7 February 2005 (07.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/541,942 6 February 2004 (06.02.2004) US
10/996,070 24 November 2004 (24.11.2004) US

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Published:

- with international search report
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

(88) Date of publication of the international search report:
2 April 2009

(54) Title: THYMIDYLATE SYNTHASE GENE AND METASTASIS

(57) Abstract: Thymidylate synthase (TYMS) gene amplification was observed in 23% of 31 5-FU resistant liver metastases, while no amplification was observed in metastases of patients that had not been treated with 5-FU. Patients with metastases containing TYMS amplification had a substantially shorter median survival (329 days) than those without amplification (1021 days, $p < 0.01$). Genetic amplification of TYMS has important implications for the management of colorectal cancer patients with recurrent disease.

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US05/03776

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07H 21/04(2006.01);C12Q 1/68(2006.01)

USPC: 435/6;536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
TS, thymidylate; 5-FU,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GORLICK et al. "Higher levels of thymidylate synthase gene expression oare observed in pulmonary as compared with hepatic metastases of colorectal adenocarcinoma." J. of Clinical Oncology, Vol. 16, No. 4, pages 1465-1469, April 1998.	1-3, 5-9, 13-15
Y		4-5, 10-12, 16-20
X	HIDAKA et al. Rinsho Byori, Vol. 199, pages 164-170, 2002.	1, 3-5
Y	ROONEY et al. "Comparative genomic hybridization analysis of choromsomal alterations induced by the development of resistance to thymidylate synthase inhibitors." Cancer Reserach, Vol. 58, pages 5042-5045, November 15, 1998.	4-5
Y	HIDAKA et al. "Chromosomal imbalances associated with acquired resistance to fluoropyrimidines in human colorectal cancer cells." Eur. J. of Cancer. Vol. 39, pages 975-980, 2003.	10-12, 16-20

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☐ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

10 December 2007 (10.12.2007)

Date of mailing of the international search report

21 DEC 2007

Name and mailing address of the ISA/US

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